CERVICAL CARCINOMA
The Role of the Human Papilloma Virus and Prospects for Primary Prevention

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MAGNITUDE OF THE PROBLEM

- Carcinoma (ca) of the cervix is the 2nd commonest female cancer in the world.
- It is the commonest cancer in developing countries.
- 500,000 new cases annually.
- 75-80% in developing countries.
- About 300,000 deaths annually.
  - 80% are from developing countries.
- Screening in developed countries has reduced cervical cancer death by 70%.
OBJECTIVES

- Literature review
  - on aetiology of ca cervix.
  - available methods for low resource settings
- Identify possible preventive measures to reduce the risk of ca cervix
METHODOLOGY

- ELECTRONIC SEARCH
  - Pubmed
  - Medline
  - Cochrane library
  - WHO and collaborative institutions
  - unpublished literature
AETIOLOGY OF CA CERVIX

- RISK FACTORS
  - early onset of sexual intercourse
  - multiple sexual partners
  - male partner’s behaviour + ca penis
  - history of ca cervix in close relatives
  - cigarette smoking
  - combined oral contraceptive pill
  - reduced immunity
AETIOLOGY OF CERVICAL CARCINOMA

- Risk factors point to an infectious process
- In the 1970s and early '80s – CMV and Herpes Simplex type 2
- Positive association between HPV and ca cervix - HPV 16 identified in 1983
- About 99.7% of Ca cervix associated with HPV infection
- Main oncogenic strains are: types 16 and 18
- Other types: 31, 33, 51, 53, 35 etc.
HPV

- Small double-stranded DNA virus with protein capsid.
- About 120 types of HPV described.
- Circular viral genome - divided into 3 regions.
  - Upstream Regulatory Region
  - Early Region - E1, E2, E3, E4, E5, E6, E7
  - Late Region - L1, L2
- E6 & E7 responsible for oncogenic properties of HPV
MODE of TRANSMISSION

- Sexually transmitted (~75% sexually active women infected).
- Genital tract micro-trauma enhance viral entry into host cells.
- Virus may live transiently in cervix or may persist according to host factors.
- Persistent infection $\rightarrow$ cervical changes
  - E6 & E7 proteins block natural control of growth of cervical cells.
  - Integration of viral genome $\rightarrow$ host cell DNA
CERVICAL CHANGES

- Mutation may occur in the cervical cell
  - $\rightarrow$ pre-cancer $\rightarrow$ cancer.
- Precancerous changes identifiable through exfoliative cytology
- Papanicolaou and Straut (1943) = Initiation of pap smear test
  - Screening with the pap smear has been used in developed countries for 50 years.
- Low resource countries cannot afford Pap smear but carry most of disease burden.
SCREENING TESTS

- PAP SMEAR
- Cervical specimen taken with spatula / brush and smeared on glass slide for examination.
- Sensitivity - 51%
- Specificity - 98%
- High false negative rate
- Liquid-based thin prep available now → better results
- Computerised system now available
- To improve on cervical precancer detection
  - HPV DNA tests (PCR / Hybrid Capture II)
SCREENING TESTS

- Pap smear very expensive for low income countries
- Highly qualified personnel needed for reading of slides and managing problems with colposcopy etc
- Effective infrastructure required
- Need for technique that is easily applied, affordable, accessible, and user friendly
SCREENING TESTS

VISUAL INSPECTION WITH ACETIC ACID (VIA).

- New method under investigation.
- Sensitivity and specificity: 76% / 64%
- Simplicity of use enables wide clinical application
- Treatment for low grade lesions can be done at same visit (cryotherapy)
- Higher grade lesions or cancer referred to hospital
SCREENING TESTS

- OTHER SCREENING METHODS
  - visual inspection with magnification (VIAM)
  - Cervicography
  - fluorescent spectroscopy
  - infra-red spectroscopy
  - polar probe
VACCINATION

- Very attractive idea (compare hepatitis B and ca liver)
- Viral capsid proteins useful - highly immunogenic hence prospects for vaccine.
- 1991 - virus-like particles developed with L1
- Immunity is type-specific hence may be difficult to develop poly-valent vaccine to prevent all oncogenic types of HPV.
- About 20 different vaccines currently under development
- WHO trials
CONCLUSION

- HPV causes ca cervix
- Screening with pap smear expensive
- HPV DNA testing also expensive
- Hope for developing countries = VIA
- VIA shown to be cost effective.
- Practising of safe sexual behaviour
THANK YOU

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